

INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Article 36 and Rule 70)

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Applicant's or agent's file reference REP06604WO		FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)	
International application No. PCT/GB 03/05368	International filing date (day/month/year) 09.12.2003	Priority date (day/month/year) 09.12.2002	
International Patent Classification (IPC) or both national classification and IPC C07D251/54			
Applicant PROMETIC BIOSCIENCES LTD. et al.			

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.

☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

 These annexes consist of a total of 1 sheets.

3. This report contains indications relating to the following items:
 - I ☒ Basis of the opinion
 - II ☐ Priority
 - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - IV ☐ Lack of unity of invention
 - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - VI ☐ Certain documents cited
 - VII ☐ Certain defects in the international application
 - VIII ☐ Certain observations on the international application

Date of submission of the demand 07.07.2004	Date of completion of this report 18.03.2005
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Kollmannsberger, M Telephone No. +49 89 2399-7364



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB 03/05368

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-28 as originally filed

Claims, Numbers

1-6 as originally filed
7-17 filed with telefax on 28.02.2005

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:
- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.
4. The amendments have resulted in the cancellation of:
- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:
5. ☒ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

see separate sheet

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6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-17 (in part)

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-17 (in part) are so unclear that no meaningful opinion could be formed (*specify*):

see separate sheet

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the Standard.

☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	6,13
	No: Claims	1-5,10-12,14-17
Inventive step (IS)	Yes: Claims	6
	No: Claims	1-5,10-17
Industrial applicability (IA)	Yes: Claims	1-17
	No: Claims	

2. Citations and explanations

see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

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Re Item I

Newly filed claims 7-9 define X as being "derived from" ammonia or various diaminoalkanes. diaminoalkanes. The respective paragraph of the description (paghe 5 first paragraph) describes these amines and states as well as that they can be modified by OH groups. Hoever, this does not form a basis for the use of "derived from" in the claims, since "derived from" does not have any structural limitations. These claims are considered to go beyond the originally filed disclosure. No opinion can be given on claims 7-9

Re Item III

The definition of the "support material M" in claim 1 is lacks support and disclosure in the description (Art. 5/6 PCT).

The meaning of this definition which according to the description can be "any suitable compound or material" (cf. page 4 of the description) has been restricted to exclude low-molecular compounds (i. e. restricted to solids or polymers) in line with the disclosure of the invention. Otherwise myriads of low molecular compounds would be novelty destroying.

Re Item V

V.1. State of the art

The following documents have been cited:

- D1: WO 01/42228 A (LOWIK DENNIS ; LOWE CHRISTOPHER ROBIN (GB); PROMETIC BIOSCIENCES LTD () 14 June 2001 (2001-06-14)
- D2: GB-A-2 053 926 (ATKINSON A; HARVEY M J) 11 February 1981 (1981-02-11)
- D3: WO 97/10887 A (NOVONORDISK AS ; AFFINITY CHROMATOGRAPHY LTD (GB); BURTON STEVEN J (GB) 27 March 1997 (1997-03-27)
- D4: WO 00/67900 A (LAWDEN KIM HILARY ; LOWE CHRISTOPHER ROBIN (GB); PROMETIC BIOSCIENCES) 16 November 2000 (2000-11-16)

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- D5: EP-A-1 319 643 (3V SIGMA SPA) 18 June 2003 (2003-06-18)
- D6: LÖWIK, D W P M; LOWE, C. R.: "Synthesis of Macrocyclic, Triazine-Based Receptor Molecules" EUROPEAN JOURNAL OF ORGANIC CHEMISTRY, 2001, pages 2825-2839, XP002274796 WEINHEIM
- D7: ZHANG, W; ET AL.: "Orthogonal Convergent Synthesis of Dendrimers Based on Melamine with One or Two Unique Surface Sites for Manipulation" JOURNAL F THE AMERICAN CHEMICAL SOCIETY, vol. 123, no. 37, 2001, pages 8914-8922, XP002274797
- D8: GB-A-2 149 808 (SANDOZ LTD) 19 June 1985 (1985-06-19)
- D9: EP-A-0 122 458 (CIBA GEIGY AG) 24 October 1984 (1984-10-24)
- D10: US-B-6 482 2551 (LAVERY AIDAN JOSEPH ET AL) 19 November 2002 (2002-11-19)
- D11: ZHANG W ET AL: "Synthesis and characterization of higher generation dendrons based on melamine using p-aminobenzylamine. Evidence for molecular recognition of Cu(II)" TETRAHEDRON LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 42, no. 32, 6 August 2001 (2001-08-06), pages 5355-5357, XP004254958 ISSN: 0040-4039
- D12: US-A-4 731 393 (HOFMANN PETER ET AL) 15 March 1988 (1988-03-15)
- D13: EP-A-0 542 374 (MINI RICERCA SCIENT TECNOLOG) 19 May 1993 (1993-05-19)

D5 is a P-document and will be ignored during the PCT phase

V-2. Novelty (Art. 33(2) PCT)

The claims are novel over D2 and D3 due to the second obligatory triazine moiety.

D1 discloses compounds according to claim 1 on solid supports (see compounds 41, 43, 44). It is noted that the drafting of claim 1 with the cascade definition of Z also includes cyclic structures. The disclosure of claims 1-5 of D1 for "R2 is a solid phase group" is thus also considered novelty destroying for the present claims 1 as well as the use claims 14-

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17, since the compounds of D1 are used for the same purposes, e.g. chromatography, protein recognition/separation etc. (see D1 page 2 lines 11-22). Also libraries of macrocycles are synthesized (see example 2) the synthesis of which inevitably proceeds via libraries as claimed in claim 12 (see scheme 6 and example 2). Also claims 10 and 11 are not novel since e. g. compounds 41 and 44 in scheme 6 have more than 2(3) triazine groups and more than 3(4) Y groups.

D2 discloses affinity chromatography materials attached via N-atoms to a solid support (cf. page 2 lines 40-45). Procion Red HE-3b can be used as a ligand (see table 1) which, if both Cl atoms are attached to the support, are included in the scope of claim 1, 12-15.

D12 disclose compounds (see e. g. examples 1-6 which are attached to PE or PP (see examples A-E) resulting in polymers included in the structure of claims 1-5, 10 and 11. It is noted that the definition of Y as "aminyll group" only requires an N atom attached to the triazine.

D13 discloses melamine-formaldehyde resins also included in the scope of claims 1-5, 10,11 for the same reason. It is additionally noted that no limit for the number of Z substituents is present in the claims, so that even "normal" melamine-formaldehyde resins are included in the structural definitions of these claims.

Claims 1-5, 10-12, 13-17 are thus not novel.

Claim 6 is novel since the this specific compound is not disclosed in the cited documents. Claim 13 is considered novel since the process for the library preparation described in D1 on page 6 lines 25-30 does not explicitly disclose the dividing step.

V-3. Inventive step (Art. 33(3) PCT)

For claims which are not novel no assessment of inventive step is possible.

Claim 13 is not considered to fulfil the requirements of Art. 33(3) PCT since it only relates to basic features of generally known split-and-mix synthesis of combinatorial libraries.

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Claim 6 defines the compound of example 8. This compound differs from the disclosure of D2-D4 in the second triazine moiety and from the end products of D1 in that it is not cyclic. D3/D4 can be seen as closest state of the art since these documents also deal with the preparation of compounds useful for e. g. purification of amminoglobulines using affinity chromatography.

The problem to be solved is thus the provision of further compounds which can be used in such a process.

Starting from D3/D4 the skilled man would not arrive at the compound of claim 6 without inventive skills since the addition of the second triazine ring and the specific structure of the compoiund of claim 6 is not suggested by the cited prior art.

Claim 6 fulfils Art. 33(3) PCT.